

Amendments to the Specification:

Please replace the paragraph beginning at page 3, line 25, with the following amended paragraph:

The present invention relates to methods and compositions for monitoring the status of and for treating ~~the status of~~ a transplanted organ in a host. In certain aspects, the present invention relates to evaluating transplant rejection in a host by determining the magnitude of gene expression in a post-transplant biological sample obtained from the host and comparing the relative expression of the marker genes to a baseline level of expression of the immune activation marker, ~~wherein upregulation~~ Upregulation of gene expression (i.e., increased or heightened gene expression) of two or more selected genes in the sample indicates rejection, and downregulation of gene expression is indicative of a ~~non-rejection~~ non-rejection state. In one aspect, the invention relates to the detection of immune activation genes such as perforin (P), granzyme B (GB), and Fas ligand (FasL). Immune activation genes are also referred to herein as cytotoxic lymphocyte (CTL) effector molecules. In another aspect, the invention relates to the detection of cytoprotective genes such as heme oxygenase-1 and A20.

Please replace the paragraph beginning at page 5, line 3, with the following amended paragraph:

In certain embodiments, the magnitude of expression of the indicator genes is determined by quantifying marker gene transcripts and comparing this quantity to the quantity of transcripts of a constitutively expressed gene. The term "magnitude of expression" means a "normalized, or standardized amount of gene expression". For example, the overall expression of all genes in cells varies (i.e., is not constant). To accurately assess whether the detection of increased mRNA transcript is significant, it is preferable to "normalize" gene expression to accurately compare levels of expression between samples. Normalization may be accomplished by determining the level of expression of the gene of interest (e.g., determining gene mRNA or cDNA transcribed from the gene mRNA) and the level of expression of a universally, or constitutively expressed gene (e.g., a gene that is present in all tissues and has a constant level of expression), and

comparing the relative levels of expression between the target gene (gene of interest) and the constitutively expressed gene. In one embodiment, the constitutively expressed gene is ~~glyceraldehyde 3-phosphate~~ glyceraldehyde-3-phosphate dehydrogenase (GAPDH). In a further embodiment, the constitutively expressed gene is cyclophilin B. Other constitutively expressed genes, such as actin, are known to those of skill in the art and can be suitable for use in the methods described herein. In exemplary methods described herein, quantification of gene transcripts was accomplished using competitive reverse transcription polymerase chain reaction (RT-PCR) and the magnitude of gene expression was determined by calculating the ratio of the quantity of gene expression of each marker gene to the quantity of gene expression of the constitutively expressed gene. That is, the magnitude of target gene expression is calculated as pg of target gene cDNA per pg of constitutively-expressed gene cDNA. In other embodiments, gene expression is measured by binding of cDNA or mRNA or fragments thereof to a nucleotide array, and preferably a microarray. In preferred embodiment the cDNA, mRNA or fragments are labeled for easier detection.

Please replace the paragraph beginning at page 6, line 10, with the following amended paragraph:

In another embodiment, the post-transplant test sample comprises a blood sample obtained from the host, the sample ~~which~~ contains peripheral blood mononuclear cells (PBMCs) ~~which and~~ and is evaluated for the marker genes. Additionally, the PBMC sample is substantially simultaneously, or sequentially, evaluated for the presence or absence of one or more genes that are characteristic of (e.g., a marker for) an infectious agent (e.g., a virus). In certain embodiments, heightened expression of one, two or more genes of any of the gene clusters of Table 1, ~~concomitant~~ concomitant with the absence of the marker for the infectious agent indicates transplant rejection. In one embodiment, heightened gene expression of two of the three immune activation marker genes, P, GB and FasL, concomitant with the absence of the marker for the infectious agent indicates acute transplant rejection. In another embodiment, heightened expression of genes belonging to the various clusters, concomitant with the absence

of the marker for the infectious agent indicates transplant rejection. For example, to evaluate acute transplant rejection of a renal allograft, the genes characteristic of the infectious agent cytomegalovirus (CMV) would be assessed. Importantly, this embodiment acts as a screening test, using easily obtained PBMCs, to differentially distinguish between acute rejection of the transplant or infection. In this case, further testing, such as with a transplant biopsy sample, will only be performed if the initial "screening" test using PBMCs is positive for rejection. Thus, transplant hosts are not submitted to invasive biopsy procedures unless it is justified (i.e., necessary to establish rejection).

Please replace the paragraph beginning at page 34, line 30, with the following amended paragraph:

For example, the cDNA of perforin can be amplified with a pair of oligonucleotide primers comprising the nucleotides of SEQ. ID. NOS.:17 and 18 of Table 1. Likewise, the transcript of ~~glyceraldehyde 3-phosphate~~ glyceraldehyde-3-phosphate dehydrogenase can be amplified with oligonucleotide primers comprising the nucleotide sequence of SEQ. ID. NOS. 1 and 2. A20, for example, can be amplified and quantified using primers selected from SEQ ID NOS: 33, 34 and 35. HO-1, for example, can be amplified with primers selected from SEQ ID NOS: 39, 40 and 41. Although these primers are specifically described herein, other suitable primers can be designed using techniques well-known to those of skill in the art. See, for example, Current Protocols in Molecular Biology, Volume 2, Ausubel et al., eds., John Wiley & Sons, Inc. (1997) at pp. 15.0.1-1-15.8.8.